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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,089	12/17/1999	Keiko Sakakibara	001560-377	1763

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EXAMINER
EINSMANN, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1634	33

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/446,089	SAKAKIBARA ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *10-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper No. 32 is acknowledged. The traversal is on the ground(s) that the invention meets the "unity of invention" standard and that the examination of the entire claim set would not pose a serious burden on the examiner. This is not found persuasive for the reasons that follow.

In the instant case, however, there is a lack of unity since the broadest claim does not provide a special technical feature over the prior art (see 102 rejections below). Although the prior art does not teach that the nucleic acid taught by Kupper *et al.* has the activity described in the claim, the fact cannot be removed that the prior art provides the nucleic acid sequence of the Neurospora tyrosinase gene. The instant claims are product claims, an the recitation of a property of the product (i.e. a new utility) does not change the fact that the claimed product is identical to that taught by Kupper *et al.* (see MPEP 2122). PCT Rule 13.2 states "The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes ***over the prior art.*** (emphasis added)" Since the DNA sequence of claim 1 is anticipated, this claim provides no special technical feature over the prior art.

Furthermore, Applicant argued that it would not be a significant burden for the examiner to examine the claims, citing MPEP 803. However, this is not persuasive because the requirements of MPEP 803 are not applicable in a 371 case. At the beginning of chapter 800, the MPEP states,

> "This chapter is limited to a discussion of the subject of restriction and double patenting under Title 35 of the United States Code and Title 37 of the Code of Federal Regulations

> as it relates to national applications filed under 35 U.S.C. 111(a). The discussion of unity of invention under the Patent Cooperation Treaty Articles and Rules as it is applied as an International Searching Authority, International Preliminary Examining Authority, and in applications entering the National Stage under 35 U.S.C. 371 as a Designated or Elected Office in the U.S. Patent and Trademark Office is covered in Chapter 1800."

Under unity of invention standards, the lack of a special techincal feature as discussed in the preceeding paragraph is sufficient to require the restriction as previously provided. Furthermore, even if the unity of invention standards did require that a showing of burden be made, it is noted that the separately grouped inventions in the restriction requirement would also be separately classified. The separate classification of the groups is *prima facie* evidence that the examination of these inventions would place an undue burden on the examiner. Applicant's arguments do not overcome such a burden.

As such, the restriction requirement is still deemed proper.

Applicant is reminded that prior to allowance non-elected subject matter must be cancelled from claim 9.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a protein having activity to synthesize aureusidin by using chalcones as substrates, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 2, does not reasonably provide enablement for any other nucleic acids

encoding such proteins, or for nucleic acids encoding proteins that have the ability to synthesize any other aurones, or for the gene encoding SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Instant claim 1 encompasses gene which encodes a protein having activity to synthesize aurones by using chalcones as substrates. Claims 2-5 depend from claim 2 and provide further limitations to the claims. Claim 2 indicates that the encoded protein is a polyphenol oxidase. Claims 3-5 each depend from claim one and recite that the claimed gene encodes SEQ ID NO: 2, or any amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2, or that the gene is capable of hybridizing under stringent conditions to SEQ ID NO: 1, or that the gene have sequence homology to SEQ ID NO: 2. Claims 6-9 recite vectors, hosts, and host cells.

The specification teaches a single cDNA molecule (SEQ ID NO: 1) which encodes the polypeptide SEQ ID NO: 2. The working examples demonstrate that the polypeptide encoded by SEQ ID NO: 1 has the ability to synthesize aureusidin by using chalcones as substrates (Examples 3 and 6). The specification further teaches that the enzyme tyrosinase form the organisms Neurospora also has the ability to synthesize aureusidin by using chalcones as substrates (Example 18). The nucleic acid encoding the Neurospora tyrosinase was known in the prior art at the time the invention was made (see Kupper *et al.* and 102(b) rejections below), an by virtue of the fact that it was known in the prior art at the time the invention was made, this nucleic acid is also considered to be enabled by the prior art. Kupper *et al.* teach both the coding sequence of the Neurospora tyrosinase and the genomic sequence. The specification also teaches

that instant SEQ ID NO: 2 has a copper binding region that is typical of the active center of polyphenol oxidases (Example 10).

The specification and the prior art are silent as to any other polypeptides that have the ability to synthesize aureusidin by using chalcones as substrates, or any polypeptides that have the ability to synthesize any other aurones (other than aureusidin) from chalcones. Neither the specification nor the prior art establish any relationship between all polypehnol oxidases and the activity that is attributed to instant SEQ ID NO: 2 and the Neurospora tyrosinase.

There are many polyphenol oxidase molecules (and nucleic acids encoding them) known in the prior art (see, for example, Hunt *et al.*, cited in paper number 30, Boss *et al.* and Robinson *et al.*, discussed below). However, neither the specification nor the prior art provide any guidance that would lead any person skilled in the art to select of all of the possibilities which nucleic acids already discovered, or yet to be discovered would possess the ability to synthesize aureusidin by using chalcones as substrates, or the ability to synthesize any other aurone using chalcones as substrates.

Furthermore, it is noted that the instant claims are drawn to include "genes" which encode proteins. The recitation "gene" encompasses full length genomic coding molecules, typically including any relevant 5' and 3' non-coding regions as well as introns and other regulatory sequences. The specification does not provide any of these sequences for the gene encoding instant SEQ ID NO: 2. Such sequences are completely unpredictable, and the acquisition of such sequences would require substantial effort on the part of the practitioner.

While the level of skill in the relevant art is quite high (PhD in biochemistry), the level of unpredictability is higher with regard to the ability to change an amino acids in a particular

sequence while still retaining the functionality of the enzyme. The specification provides absolutely no guidance as to which or how many of the amino acids of instant SEQ ID NO: 2 can be changed yet still result in a polypeptide which retains the ability to synthesize aureusidin by using chalcones as substrates. Further, the specification gives no guidance as to the structure or identity of nucleic acids encoding any other sequence that has the ability to synthesize aurones other than aureusidin.

The identification of other nucleic acids that fall within the scope of the instantly claimed invention would require the screening of every possible enzyme to determine if they have the recited functionality. Such a search would be complicated by the fact that the skilled artisin would have no guidance as to which enzymes which are known or unknown would fall within the scope of the claimed invention.

Because of the breadth of the claims, the provision of only two sequences with the ability to synthesize aureusidin by using chalcones as substrates, the lack of any showing that other aurones could be synthesized, the fact that full length genes are not provided which encode polypepetides shown to have the ability to synthesize aureusidin by using chalcones as substrates, the lack of direction in the specification of the identity and structure of other such enzymes, and the large quantity of experimentation necessary to identify other members of the claimed group, it is concluded that undue experimentation would be necessary to practice the claimed invention commensurate in scope with the instantly rejected claims.

4. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claim 1 encompasses gene which encodes a protein having activity to synthesize aurones by using chalcones as substrates. Claims 2-5 depend from claim 2 and provide further limitations to the claims. Claim 2 indicates that the encoded protein is a polyphenol oxidase. Claims 3-5 each depend from claim one and recite that the claimed gene encodes SEQ ID NO: 2, or any amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2, or that the gene is capable of hybridizing under stringent conditions to SEQ ID NO: 1, or that the gene have sequence homology to SEQ ID NO: 2. Claims 6-9 recite vectors, hosts, and host cells.

This large genus is represented in the specification by one species, the nucleic acid encoding SEQ ID NO: 2. Claim 1 is so broad as to encompass nucleic acids encoding any possible enzyme that has the recited activity. The claim provides no structure to define the claimed nucleic acid. Claim 2 requires that the enzyme is a polyphenol oxidase, but still, provides no structure to define the claimed invention. Claim 3 recites a nucleic acid encoding SEQ ID NO: 2, but then allows that the nucleic acid can also encode a polypeptide modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2, with no limit to the number of deletions, substitutions or additions. Essentially, the claim 3 provides no further structural limitation to the subject matter of claim 1 because claim 3 allows for an unlimited number of changes to the reference sequence. Claim 4 makes no requirement as to the stringency of hybridization SEQ ID NO: 1, and thus, the claim encompasses any nucleic acid having the recited function that would hybridize to SEQ ID NO: 1 under any possible conditions.

Thus, applicant is in possession of nucleic acids encoding only a single amino acid sequence, that is SEQ ID NO: 2.

The instant claims are also drawn to genes, and encompass, therefore, genomic coding sequences. Such a sequence includes 5' and 3' untranslated regions, introns, and other regulatory sequences. However, applicant has only described the coding portion of the nucleic acid encoding SEQ ID NO: 2.

As noted in the scope of enablement rejection, the specification does not teach a nucleic acid that has the ability to synthesize any aurone except aureusidin. With regard to the functional requirement of the claims, applicant is in possession only of nucleic acids encoding SEQ ID NO: 2 which has the activity to synthesize aureusidin from chalcones.

Thus, applicant has express possession of only one species in a genus which comprises hundreds of millions of different possibilities.

With regard to the written description, all of these claims encompass nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claim 5 includes modifications by permitted by the % identity language for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only nucleic acids encoding instant SEQ ID NO: 2 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids that encode proteins modified by addition, insertion, deletion, substitution or inversion with respect to the disclosed SEQ ID No: 2 such that a different amino acid sequence is encoded which has the activity to synthesize aureusidin from chalcones.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 4, 5, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite over the recitation of "capable of hybridizing" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited nucleic acids have the potential to hybridize or do in fact hybridize the recited sequence. Amendment of the claim to read, for example, "which hybridizes" would obviate this rejection.

Claim 4 is indefinite over the recitation "under stringent conditions" because it is not clear how this recitation is limiting to the claims since essentially all hybridization conditions are

stringent, but it is the level of stringency that varies between conditions (i.e., high stringency versus low stringency).

Claim 5 is indefinite over "having sequence homology relative to the amino acid sequence described in SEQ ID NO: 2" a gene is a nucleic acid and it is not clear how a nucleic acid can have sequence homology to an amino acid.

Claim 7 is indefinite because it is not clear what applicant intends by "host." Such language encompasses, for example, transgenic animals which are transformed with the claimed vectors, yet the specification does not discuss such transgenic animals. Amendment of the claim, for example, to recite a "host cell" will obviate this rejection. (Amendment to recite a "host cell" or a "host plant" would also overcome this rejection, but the "host plant" would encompass non-elected subject matter).

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to genes encoding proteins having recited activity, but the claims do not include any language which indicates that the contemplated subject matter is isolated from its natural form. Because the claims read on polynucleotides that would occur in nature, untouched by the hand of man, these claims, as broadly drawn, encompass non-statutory subject matter. This rejection may be overcome by amendment of the claims to include, for example, language clarifying that the claimed nucleic acids are intended to be isolated and/or purified nucleic acids.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 2, 3, 4, 5, 6, 7, and 8 rejected under 35 U.S.C. 102(b) as being anticipated by Kupper *et al.* (The Journal of Biological Chemistry, 1989, Vol. 264, No. 29, p. 17250-17258).

Kupper *et al.* teach a nucleic acid encoding a protein having activity to synthesize aurones by using chalcones as substrates. Specifically, Kupper *et al.* teach the gene encoding tyrosinase from Neurospora (Figure 7). This nucleic acid encodes a polypeptide that has the

activity to synthesize aurones by using chalcones as substrates. The encoded polypeptide is an amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2. The polynucleotide taught by Kupper *et al.* is capable of hybridizing to instant SEQ ID NO: 1 under some stringency conditions, even if those conditions be very low. With regard to claim 5, this reference is applied because it is not clear what the claim encompasses, but the polynucleotide meets the functional limitaitons of the claim. Kupper *et al.* teach vectors comprising the nucleic acid encoding tyrosinase, as well as E.coli host cells transformed by such vectors (p. 17257).

It is noted that Kupper *et al.* do not teach that tyrosinase from Neurospora has the activity of synthesizing aurones by using chalcones, however, this ability is an inherent property of the tyrosinase whose gene is taught by Kupper *et al.* This functionality was in fact confirmed in Example 18 of the instant specification. Applicant is reminded that "The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable (MPEP 2112)."

11. Claims 1-9 are rejected under 35 U.S.C. 102(e) as anticipated by Robinson (US 6242221).

Robinson teaches nucleic acids encoding polyphenol oxidases. The nucleic acid taught by Robinson as SEQ ID NO: 7 encodes a polypeptide having 64% identity with instant SEQ ID NO: 2. The encoded polypeptide is an amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2. The polynucleotide taught by Kupper *et al.* is capable of hybridizing to instant SEQ ID NO: 1 under some stringency conditions, even if those conditions be very low. Robinson does not teach that the polyphenol

oxidase encoded by their SEQ ID NO: 11 has the activity to synthesize aurones from chalcones. However, the instant specification teaches that "enzymes having polyphenol oxidase activity clearly have activity to synthesize aurones by using chalcones as substrates (p. 8)." Because the nucleic acid taught by Robinson is a polyphenol oxidase, and because it encodes a polypeptide having greater than 50% identity to instant SEQ ID NO: 2, the nucleic acid taught by Robinson appears to be identical to the claimed nucleic acid. Robinson *et al.* further teach host cells from microorganisms and plants which are transformed by a vector comprising the polyphenol oxidase genes (Col. 9-10).

12. Claims 1-7 and 9 are rejected under 35 U.S.C. 102(b) as anticipated by McBride *et al.* (WO 96/40951).

McBride *et al.* teach a nucleic acid encoding a protein having activity to synthesize aurones by using chalcones as substrates. Specifically, McBride *et al.* teach vectors comprising genes encoding tyrosinase and ORF438 from Streptomyces antibioticus (see p. 26, lines 18-29 and example 10). The encoded polypeptide is an amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2. The polynucleotide taught by McBride *et al.* is capable of hybridizing to instant SEQ ID NO: 1 under some stringency conditions, even if those conditions be very low. With regard to claim 5, this reference is applied because it is not clear what the claim encompasses, but the polynucleotide meets the functional limitaitons of the claim. McBride *et al.* teach vectors comprising the nucleic acid encoding tyrosinase, as well as E.coli and plant host cells transformed by such vectors (Example 11).

It is noted that McBride *et al.* do not teach that this tyrosinase from has the activity of synthesizing aurones by using chalcones, however, the polypeptide encoded by the nucleic acid taught by McBride *et al.* is a tyrosinase, and the instant specification teaches that at least one tyrosinase meets the functional requirements of the instant claims. Furthermore, McBride *et al.* observed transgenic plants that exhibited an alteration in plant color (some meristem yellowing), which would result from the described activity (p. 56). Thus, the nucleic acid taught by McBride *et al.* appears to be identical to the claimed nucleic acid.

Conclusion

13. No claims are allowed

14. A claim drawn to an isolated nucleic acid encoding SEQ ID NO: 2 would be free of the prior art and would be free of all of the other rejections of record.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C. Einsmann
Examiner
Art Unit 1634

February 22, 2002